
Evidence against a Stem Cell Origin of New Hepatocytes in a Common Mouse Model of Chronic Liver Injury.

Journal: Cell Rep

Publication Year: 2014

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PubMed link: 25131204

Funding Grants: Molecular dissection of adult liver regeneration to guide the generation of hepatocytes from pluripotent stem cells

Public Summary:

Hepatocytes, the cells of the liver that provide most of its functions, typically regenerate themselves. However, in chronic liver diseases the regenerative capabilities of hepatocytes can be overwhelmed. Under these conditions liver stem cells are thought to serve as a backup system by producing new hepatocytes. Our study failed to find evidence for liver stem cell-derived hepatocytes in mice, which argues against the existence of liver stem cells and highlights the importance of the regenerative capabilities of hepatocytes.

Scientific Abstract:

Hepatocytes provide most liver functions, but they can also proliferate and regenerate the liver after injury. However, under some liver injury conditions, particularly chronic liver injury where hepatocyte proliferation is impaired, liver stem cells (LSCs) are thought to replenish lost hepatocytes. Conflicting results have been reported about the identity of LSCs and their contribution to liver regeneration. To address this uncertainty, we followed candidate LSC populations by genetic fate tracing in adult mice with chronic liver injury due to a choline-deficient, ethionine-supplemented diet. In contrast to previous studies, we failed to detect hepatocytes derived from biliary epithelial cells or mesenchymal liver cells beyond a negligible frequency. In fact, we failed to detect hepatocytes that were not derived from pre-existing hepatocytes. In conclusion, our findings argue against LSCs, or other nonhepatocyte cell types, providing a backup system for hepatocyte regeneration in this common mouse model of chronic liver injury.

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